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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SAUCIER, SANDRA E

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/890,654	Applicant(s) Nowak et al.
	Examiner Sandra Saucier	Art Unit 1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 9, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above, claim(s) *1-8 and 13* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *9-12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-13 are pending. Claims 9-12 are considered on the merits. Claims 1-8 and 13 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Claims 1-8 and 13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected , the requirement having been traversed in Paper No. 8.

The traversal is on the grounds that a) Group II is a kit used to carry out the method of Group I and thus has unity of invention with the method of use, and b) no serious burden has been demonstrated.

a) In addition to the requirement that a group of inventions must belong to one of the specific categories provided by PCT Rule 13.2, the inventions in the category, such as a composition and a method of use of the composition, must have a special technical feature that unites them. See Patent Rule §1.475, where a special technical feature is defined as a contribution OVER THE PRIOR ART. Since the composition AS CLAIMED has been shown to be known in the art in paper # 7 as explained below in the anticipatory rejection over Han *et al.*, no special technical feature unites these inventions in a category.

b) Under a USC 371 filing, burden is not an element that must be demonstrated for a proper restriction.

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 recite "not interfering in the transformation prothrombin/active meizothrombin or Mtdesfgl, resp." and "dissociable by active meizothrombin or Mtdesfgl, resp.", "dissociating prothrombin into meizothrombin or Mtdesfgl, resp.".

It is unclear what these recitations mean because a) a slash is used to separate words. Are the words meant to be alternatives or synonyms or some other relationship? b) "of" appears to be missing before prothrombin in the first recitation c) an abbreviation "Mtdesfg1" is used without properly referencing or defining it; this abbreviation does not appear to be a recognized term of art and there is no reason to capitalize it, d) what does the "resp." mean, if it means respectively, with respect to what?

Further, it is uncertain whether the recitation "wherein component K3 may be replaced or complemented by a component K3a of a solution with meizothrombin or Mtdesfg1, resp." is intended to further limit or expand the components of the claimed composition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 10 and 12 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Han *et al.* [AU].

The claims are directed to a kit comprising:
1) a solution of a coagulation-inhibiting substance not interfering in the transformation prothrombin/active meizothrombin or Mtdesfgl, resp.
2) a chromogenic or fluorogenic substance dissociable by active meizothrombin or Mtdesfgl, resp.
3) a solution of a substance dissociating prothrombin into meizothrombin or Mtdesfgl, resp.
4) wherein component 3 may be replaced or complemented by meizothrombin or Mtdesfgl, resp.

Claim 10 recites "as an option" before reciting all the components. Thus, the claim is interpreted to have no components "as an option".

Claim 12 recites "as an optional additional kit component..." and is interpreted to not exercise that option and have only components K1, K2 and K3.

The references are relied upon as explained below.

Han *et al.* disclose components comprising 1) antithrombin, 2) tosyl-Gly-Pro-Arg-p-nitroanilide and 3) factors Xa, Va and phospholipid. They are used in a test of inhibition of prothrombin activation products by antithrombin (Fig. 4).

Insofar as the composition claims rely on the inclusion of components which instead of being characterized by technical features suitable for the identification of components which are compounds, is imprecisely defined by means of functional features which merely recite the desired result to be achieved, the subject matter is considered to be anticipated by the disclosure of the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Han *et al.* [AU].

The claim is directed to the separation of the components in a single kit package.

Han *et al.* has been explained above.

It is considered to be well within the purview of one of skill in the art to separately package components within a single package. All of the components as claimed are known in the prior art and are used for the same purpose as the instant purpose, that is, for investigation of coagulation processes. Patentability which depends on non-specific packaging should show evidence of criticality in order to overcome an rejection of obviousness.

One of ordinary skill in the art would have been motivated at the time of invention to make this division and packaging of reagents in order to obtain the resulting composition or kit as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,547,850 [AA] in light of US 5,702,912 [A] or Houbouyan *et al.* [U].

The claims are directed to a kit comprising:
1) a solution of a coagulation-inhibiting substance not interfering in the transformation prothrombin/active meizothrombin or Mtdesfg1, resp. such as heparin,
2) a chromogenic or fluorogenic substance dissociable by active meizothrombin or Mtdesfg1, resp. such as a p-nitroanilide type substrate,
3) a solution of a substance dissociating prothrombin into meizothrombin or Mtdesfg1, resp., such as ecarin,
4) wherein component 3 may be replaced or complemented by meizothrombin or Mtdesfg1, resp.

Claim 11 is directed to the separation of the three or four components and their packaging in a single test kit.

Claim 12 is directed to the inclusion of a separate solution of prothrombin as another component in the test kit.

US 5,547,850 discloses a composition comprising:

1) heparin,
2)
3) ecarin,
4) meizothrombin and/or meizothrombin-des-fragment 1 (col. 2, l. 26-33).

The composition is used for the determination of hirudin and other thrombin inhibitors.

The composition lacks (2) the chromogenic substrate which produces p-nitroanilide for spectrographic analysis and the inclusion of a separate vial of prothrombin.

The detection of the end point of the reaction is performed with an electrically triggered coagulation test (col. 3, l. 39). This test is also known as the ecarin clotting time test.

US 5,702,912 discloses an assay for determining the concentration of inhibitors of thrombin where the assay for the activity of thrombin may be either a coagulation (clotting) test or a chromogenic substrate for thrombin such as S2238 (Kabi) which is read spectroscopically (col. 5, l. 61-67). The reagents are:
1) clotting factor reagent comprising prothrombin, antithrombin III,
2) chromogenic substrate for thrombin (S2238) and EDTA and
3) activator

Houbouyan *et al.* disclose the equivalency of the chromogenic method of detection (amidolytic method) which is read spectroscopically and the clotting end point for the determination of the concentration of thrombin inhibitors present in a sample. Both measure thrombin activity. The chromogenic substrate is S2238 which releases p-nitroanilide for spectroscopic analysis at 405nm.

The substitution of the chromogenic assay for the clotting assay in the method of '850 would have been obvious when taken with '912 or Houbouyan *et al.* who disclose the equivalency of such a substitution for the determination of thrombin activity. Therefore, the addition of a chromogenic substrate to the composition of '850 in order to detect the activity of thrombin spectroscopically

in a chromogenic assay instead of a clotting end point would have been obvious.

The addition of an individual solution of prothrombin to the kit would have been obvious as it may be used with hiruden or analogs of hiruden to generate standard curves in non-plasma samples which may not have sufficient native prothrombin concentrations for performance of the assay or it may be used for the generation of the meizothrombin or meizothrombin-des-fragment 1 with ecarin for use in the assay.

One of skill in the art may detect the activity of thrombin in any manner known in the art for the performance of an ecarin-mediated, thrombin inhibitor test as suggested by the references with a reasonable expectation of success.

Further, the placing of individual vials of the three to five reagents and the assembling of them into a single packaging unit is considered to be well within the purview of one of ordinary skill in the art in the absence of evidence to the contrary.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743. The normal work schedule for Examiner Saucier is 8:30 AM to 5:00 PM Monday and Tuesday and 8:30 AM to noon on Wednesday.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Customer Service Desk at (703) 308-0197 or (703)-308-0198. The number of the Fax Center for the faxing of official papers is (703) 872-9306 or for after finals (703) 872-9307.

Sandra Saucier
Primary Examiner
Art Unit 1651
June 11, 2003